REMARKS

Claims 1 - 11 are pending and are rejected. Applicant respectfully requests reconsideration in view of the following arguments.

Applicant requests consideration of reference A.L. cited on Form PTO-1449, received on February 20, 2002, which the Examiner has marked as Paper No. 4.

CLAIM REJECTIONS 35 U.S.C. §112

Claims 1-11 are rejected under 35 U.S.C. §112, first paragraph, as not enabled, because the specification does not disclose a specific use, data, examples, scientific reasoning, or *in vivo* or *in vitro* evidence of use of the invention.

The standard for enablement is whether a person skilled in the art would be enabled to practice the invention commensurate in scope with the claims (Item 2 of Office Action, 1st paragraph 2a). A patent is enabling when the disclosures made in the patent application are sufficient to allow a person skilled in the art to make and use the claimed invention. 35 U.S.C. §112, first paragraph, does not require working examples. M.P.E.P. §2164.08; *In re Strahilevitz*, 212 U.S.P.Q. 561 (C.C.P.A. 1982). To determine whether the disclosure is enabling, a two-part analysis is employed: delimiting the scope of the claimed invention, then looking to the disclosures to ascertain whether, given that level of disclosure, a person skilled in the art could successfully reproduce the claimed invention in its entire scope. *DeGeorge v. Bernier*, 226 U.S.P.Q. 758 (Fed. Cir. 1985)

The claims are directed to a method of modulating (decreasing) a cytokine-mediated hepatic injury response by administering compound-D (claim 1), a method for treating hepatic injury caused by a chemical toxin by administering compound-D (claim 8), and a method for treating bacterial or viral infection-related hepatic injury by administering compound-D.

As described at page 1, line 12 to page 2, line 2, hepatic injury results from an inflammatory or cytokine response produced by the liver in response to an insult. In other words, it is the inflammatory or cytokine response, not the original insult, that causes the resulting hepatic injury. Thus, modulating this response can lessen the injury that would otherwise occur after an insult. This is explained in the background of the application. The cause of the particular liver insult may be by a variety of mechanisms (chemical, physical, bacterial, etc.) as long as it triggers the liver's inflammatory or cytokine response. It is this method to which the claims are directed.

Applicants respectfully assert that the specification fully enables the inventive method for modulating or treating this hepatic injury response, because applicants have disclosed which compounds to use, how to administer them, the duration in which to administer them and when to stop administering them, and under which clinical conditions they should be administered. This disclosure enables the claimed invention.

At page 3, lines 10-22, the specification discloses that the peptide identified as SEQ ID NO:1 is administered. Applicants' claims recite administering a pharmaceutically acceptable formulation of SEQ ID NO:1.

Applicants have further described that this peptide may be obtained by isolating it from a natural source as known to one skilled in the art, or by synthesizing it using an automated peptide synthesizer, or by recombinant techniques (page 3, lines 5-8). Thus, one skilled in the art would be able to obtain the peptide used in the disclosed method.

The specification further describes how to administer the peptide. The specification describes the formulations (1:1:1 ethanol:propylene glycol:sodium hydroxide (1 N) with saline, adjusted to pH 7.4, as an emulsion or a solution) (page 3, lines 9-13 and 22-25), the delivery routes (any route, with parenteral routes preferred, e.g. intravenous, intramuscular, intradermal, or intraperitoneal injections) (page 3, lines 14-15; and line 25 to page 4, line 3); the dose (0.5 mg/kg to 20 mg/kg) (page 3, lines 15-17; page 4, lines 3-4); and the time of dosing (preferably prior to the start of cytokine activation, but also with or after the induction of cytokine activation) (page 4, lines 4-8). Thus, one skilled in the art would be able to dose the individual to be treated.

The specification further describes the duration of treatment. As disclosed at page 4, lines 9-11, the specification describes that the treatment should be continued on a daily basis until hepatic function normalizes, and preferably until hepatic function remains normal for at least one to two days. The specification also describes the clinical laboratory tests and provides the normal values for ascertaining normal hepatic function (hepatic enzyme profiles, albumin level, bilirubin concentration) (page 4, lines 11-19).

The specification further describes th how th inv ntiv treatm nt will be useful. At page 4, line 21 to page 5, lin 11, th specification discloses the variety of ways in which hepatic function may be perturbed, both by general categories (trauma, physical insult, chemical insult, stress, inflammation, toxicity and disease as examples) and using specific etiologies (alcoholic liver disease, *Shigella* infection, metabolic liver disease, are a few of the disclosed causative agents). Thus, the specification teaches the clinical presentation of the mammal so that one skilled in the art would know to turn to the inventive method to modulate or treat the resultant cytokine-mediated injury.

Thus, applicants respectfully assert that one skilled in this art, armed with the teachings of the specification, would be fully enabled to carry out the method of modulating a cytokine-mediated response to hepatic injury, because one skilled in the art would have know which compounds to use, how to administer them, how long to administer them and when they may stop administering them, and what clinical conditions to look for in deciding if they should be administered.

The Examiner states that the specification does not disclose which cytokines and/or which cytokine cascade steps are modulated by the peptide. Applicants respectfully assert that the invention is directed to modulating a cytokine-mediated hepatic injury response, not identification of the cytokine and/or cytokine cascade steps. The nature of the invention is a consideration in determining whether a disclosure is enabling. *In re Wertheim* 191 U.S.P.Q. 90 (C.C.P.A. 1976) (sufficiency of description depends on nature of invention and

amount of knowledge imparted to a p rson or ordinary skill in the art). Thus, there is no undue experimentation with respect to which cytokines the peptide modulates, which cascade steps are involved, etc. because these considerations are not necessary to practice the full scope of the claimed method to modulate cytokine-mediated hepatic injury.

Claims 1-11 are rejected under 35 U.S.C. §112, second paragraph, as indefinite. Applicants have amended the claims to render them sufficiently definite.

CONCLUSION

In view of the foregoing reasons, applicants submit that the claims are in condition for allowance and respectfully request a Notice of Allowance.

Applicant does not believe any fee is due with this submission. However, the Examiner is authorized to charge any fees or credit any overpayment to Deposit Account No. 23-3000.

The Examiner is invited to telephone the undersigned attorney if there are any outstanding questions or issues.

Respectfully submitted,

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